UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION
OFFICE OF PESTICIDE PROGRAMS
REGISTRATION DIVISION (7505P)

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- Contains Confidential Business Information -

DP BARCODE No.: 458531; **EPA FILE SYMBOL**: 33427-RE; **PRODUCT NAME**: Aceto Etoxazole Technical; **DECISION No.**: 559096; **PC Code(s)**: 107091; **ACTION CODE**: R334; **FOOD Use**: Yes

DATE OUT: December 2, 2020

SUBJECT: Product Chemistry Review for "*Aceto Etoxazole Technical*."
-Unregistered Source of the Active Ingredient
-Substantially Similar ("Me-Too") Registration Claim

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THROUGH: Shyam Mathur, Ph.D. sbmathur 12-02-2020
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TO: Marianne Lewis/Venus Eagle, RM #1
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INTRODUCTION:

Product & Regulatory Associates, LLC, On Behalf of Aceto US, LLC, has submitted an application dated December 13, 2019 for the registration of the new technical product "*Aceto Etoxazole Technical*." The Registrant is claiming this product is substantially similar to EPA Reg No 59639-107 ("*Valent's Etoxazole Technical*"). In support of the registration application, the Registrant has submitted Product Chemistry data with MRID Nos. 510084-01 through -04 and cited data with MRID Nos. 450899-02, -03. A proposed Confidential Statement of Formula (CSF; dated 11-26-2019) for the Basic formulation has also been submitted for review. CITAB (Chemistry) has been asked to determine acceptability of the supporting data submitted with this application.

-NO CITAB-CHEMISTRY Completeness Screen Due to Time Constraints

-NOTE: Data Evaluation Record ("Review") prepared by Summitec Corporation and amended/revised as deemed appropriate by CITAB – CHEMISTRY.

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SUMMARY OF FINDINGS:

1. Group A Guidelines: Product Chemistry Data - Product Identity, Composition, and Analysis

830.1550: Product Identity & Composition

The active ingredient was adequately described (MRID No. 510084-01). The nominal concentration of the active ingredient (99.36%, from the proposed Basic CSF dated 11/26/2019) is close to the average derived from the five-batch preliminary analysis results (99.06%, refer to Page 18 in MRID No. 51008402). The content of the active ingredient given on the proposed Basic CSF matches that stated on the product label. The product chemistry data submitted for Guideline 830.1550 satisfy the data requirements of 40 CFR §158.320.

830.1600: Description of Materials Used to Produce the Product

Material Safety Data Sheets (MSDSs) of all the starting materials, and their suppliers and specifications were provided in the study (MRID No. 510084-01). The product chemistry data submitted for Guideline 830.1600 satisfy the data requirements of 40 CFR §158.325.

830.1620: Description of Production Process

A description of the production process, chemical pathways and equipment used were provided in MRID No. 510084-01. The product chemistry data submitted for Guideline 830.1620 satisfy the data requirements of 40 CFR §158.330.

830.1670: Discussion of the Formation of Impurities

Potential impurities were identified and quantified as part of the five-batch preliminary analysis (MRID No. 510084-02). [redacted] impurities were found to be present at average levels [redacted] The formation of the impurities was fully discussed (MRID No. 510084-01). There are no impurities of toxicological significance in Aceto Etoxazole Technical. The product chemistry data submitted for Guideline 830.1670 satisfy the data requirements of 40 CFR §158.340.

830.1700: Preliminary Analysis

The five-batch preliminary analysis of Aceto Etoxazole Technical was conducted by Analytical & Regulatory Chemistry, Inc. (2395 Cains Mill Road, Sumter, South Carolina 29154). The content of the active ingredient was determined using HPLC-UV with external standard calibration which was validated with respect to linearity and precision (MRID No. 510084-02). The concentrations of the active ingredient in the five batches were: 99.04, 99.07, 98.76, 99.04, and 99.40% (average 99.06%, from Page 18 in MRID No. 510084-02). Certificates of analysis for all five batches were provided in MRID No. 510084-02. The product chemistry data submitted for Guideline 830.1700 satisfy the data requirements of 40 CFR §158.345.

830.1750: Certified Limits

The proposed upper and lower certified limits for the active ingredient are within the range of the guideline OCSPP 830.1750 recommendation. The upper certified limits for the impurities have been expanded to cover their respective highest levels detected in the five-batch preliminary analysis or to account for manufacturing variability. The nominal concentrations of the impurities listed on the proposed Basic CSF are the same as their respective averages derived from the five-batch preliminary analysis results. The Registrant proposed a nominal concentration for the active ingredient so that the concentrations for all the ingredients listed on the Basic CSF would add up to 100%. The product chemistry data submitted for Guideline 830.1750 satisfy the data requirements of 40 CFR §158.350.

830.1800: Enforcement Analytical Method

The analytical method employed to quantify the active ingredient in Aceto Etoxazole Technical was HPLC-UV with external standard calibration, which was validated (MRID No. 510084-02). The identification for the active ingredient was performed by using HPLC-UV and LC-MS against Etoxazole analytical standard (MRID No. 510084-02). The analytical methods used to determine the amounts of the impurities were provided in MRID No. 510084-02 (refer to "*830.1700: Preliminary Analysis*" under section "*Confidential Appendix*" for a summary of the methods). The product chemistry data submitted for Guideline 830.1800 do not satisfy the data requirements of 40 CFR §158.355.

2. Group B Guidelines: Product Chemistry Data – Physical and Chemical Characteristics

Adequate data were submitted for color, physical state, odor, stability to normal/elevated temperatures, oxidation/reduction, pH, melting point, UV/Visible absorption, density, partition coefficient, water solubility and vapor pressure (MRID No. 510084-03). Waivers were requested for storage stability, corrosion characteristics and dissociation constants in water (MRID No. 510084-04). No data were provided for stability to metals/metal ions, flammability, explodability, miscibility, viscosity, and boiling point as they are irrelevant to the product.

CONCLUSIONS:

The CITAB has reviewed the supporting Product Chemistry data for Aceto Etoxazole Technical and has concluded that:

1. The proposed Basic CSF (dated 11-26-2019) is acceptable. It is attached to this review.

2. The Product Chemistry data submitted for Group A Guidelines is acceptable.

3. The Product Chemistry data submitted for Group B Guidelines is acceptable.

4. The proposed product is substantially similar to the cited product.

830.1550: Product Identity & Composition
(MRID No. 510084-01)

Common Name: Etoxazole

Name:

IUPAC: (RS)-5-*tert*-butyl-2-[2-(2,6-difluorophenyl)-4,5-dihydro-1,3-oxazol-4-yl]phenetole

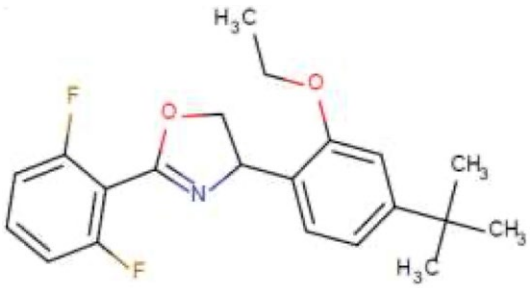
CAS: 2-(2,6-difluorophenyl)-4-[4-(1,1-dimethylethyl)-2-ethoxyphenyl]-4,5-dihydrooxazole

CAS Number: 153233-91-1

Molecular Formula: $C_{21}H_{23}F_2NO_2$

Molecular Weight: 359.41 g/mol

Structure:



830.1800: Enforcement Analytical Method
(MRID No. 510084-02)

The active ingredient in Aceto Etoxazole Technical was quantified by using HPLC-UV at 225 nm with external standard calibration (Method ARC-OP-MTH-363-P), which was validated. The identification for the active ingredient was performed based on retention time, elution pattern and MS spectrum matching by using HPLC-UV and LC-MS respectively against Etoxazole analytical standard.

The samples of Aceto Etoxazole Technical were dissolved in acetonitrile and then separated by HPLC using the following chromatographic conditions. Details provided in MRID No. 51008402, pp. 12 – 13. The retention time for Etoxazole was approximately 7.21 minutes.

Instrument: Agilent 1290 HPLC

Parameter	Value
Mobile Phase A	0.1% Phosphoric Acid
Mobile Phase B	Acetonitrile
Flow Rate	1.0 ml/min
Sample solvent	Acetonitrile
Column	Kinetex EVO C-18 4.6 x 150 mm, 2.6 um or equivalent
Column Temperature	35˚C
Autosampler Temperature	Off
Injection Volume	2 uL
Wavelength	225 nm
Run Time	20 mins

Gradient Table:

Time (mins)	Mobile Phase A	Mobile Phase B	Change
initial	50	50	-
0.5	50	50	linear
10.0	10	90	linear
13.0	10	90	linear
15.0	50	50	linear
20.0	50	50	linear

The content of the active ingredient (% w/w) in Aceto Etoxazole Technical was calculated by using the formula below.

% Assay = Sample Response /Avg Std Response x % Purity of Std

Where:

Sample Response = Average Sample Peak Area/Sample Conc (mg/mL)

Avg Std Response = Average Std Peak Area /Std Conc (mg/mL)

A summary of the method validation data for quantifying the active ingredient is presented in the table below.

Components		**Results**[a]
Linearity of response	Correlation Coefficient	0.999997
	Range of Linearity	0.020270 - 0.60810 mg/mL
Precision (% RSD)		0.11
Accuracy (% Recovery)		No data provided

[a] Data are from MRID No. 510084-02, pp. 12 and 16, and Confidential Attachment (pp. 41 – 42)

CONFIDENTIAL APPENDIX:

Group A: Product Chemistry Data – Product Identity, Composition, and Analysis

Guideline Number	Study Title	MRID Number	CITAB's Assessment	Details/Comments
830.1550	Product Identity & Composition	510084-01	A	-Adequately described -MSDSs provided
830.1600	Description of Materials Used to Produce the Product	510084-01	A	Specifications provided
830.1620	Description of Production Process	510084-01	A	Detailed description provided
830.1670	Discussion of Formation of Impurities	510084-01	A	Identities & origins of potential impurities provided
830.1700	Preliminary Analysis	510084-02	A	Five-batch analysis of the active ingredient & impurities provided
830.1750	Certified Limits	510084-01	A	-Basic CSF (11-26-2019) -Justified limits
830.1800	Enforcement Analytical Method	510084-02	A	-HPLC-UV & LC-MS -Validated

A = Acceptance; N = Not Acceptable; G = Data Gap; W = Waiver Request; NA = Not applicable; I = In Progress; U = Upgradeable

Group B: Product Chemistry Data – Physical and Chemical Characteristics

Guideline Number	Study Title	MRID Number	CITAB's Assessment	Value or Qualitative Description
830.6302	Color	510084-03	A	Light cream
830.6303	Physical state	510084-03	A	Solid - Powder
830.6304	Odor	510084-03	A	Bitter odor
830.6313 830.6317	Stability to Normal & Elevated Temperatures, Metal, & Metal Ions	510084-03	A	-Stable @ RT & 54 °C for 2 weeks (glass) -Not expected to come into contact with metals and metal ions during storage
830.6314	Oxidation/Reduction	510084-03	A	Compat ble: H_2O, $NH_4H_2PO_4$, Fe powder, $KMnO_4$ & Aromatic 200 Fluid
830.6315	Flammability	510084-04	NA	NA- Does not contain combustible liquids
830.6316	Explodability	510084-04	NA	NA - Does not contain explosive components
830.6317	Storage Stability	510084-04	A	Stable @ RT & 54 °C for 2 weeks (MRID No. 510084-03 will be used)
830.6319	Miscibility	510084-04	NA	NA – Not an EC end use product
830.6320	Corrosion Characteristics	510084-04	A	Stable @ RT & 54 °C for 2 weeks (MRID No. 510084-03 will be used)
830.6321	Dielectric Breakdown Voltage	510084-04	NA	NA – No data submitted
830.7000	pH	510084-03	A	5.44 @ 25.0 C (1% solution)
830.7050	UV/Visible Absorption	510084-03	A	Conditions / λ_{max} (nm) / ε (L/mol.cm): Neutral: 202.68 / 34000; 233.43 / 6900; 272.79 / 1900; 278.67 / 1600 Acidic: 201.33 / 64000; 232.34 / 16000 Basic: 217.33 / 23000; 272.60 / 4100
830.7100	Viscosity	510084-04	NA	NA - Product is a solid
830.7200	Melting Point	510084-03	A	100.0 - 103.0 C
830.7220	Boiling Point	510084-04	NA	NA - Product is a solid
830.7300	Density	510084-03	A	1.256 g/mL @ 22 C
830.7370	Dissociation Constant in Water	510084-04	NA	NA – Does not dissociate in water
830.7520	Particle Size & Related	510084-04	NA	NA – No data submitted
830.7550 830.7560 830.7570	Partition Coefficient (n-Octanol/Water)	510084-04 450899-02	A	Log Pow = 5.52 @ 20 C
830.7840 830.7860	Solubility – Water Solubility – Organic Solvents	510084-04 450899-02 450899-03	A	3.99×10^{-5} g/L in distilled water @ 10 C 7.04×10^{-5} g/L in distilled water @ 20 C 6.69×10^{-5} g/L in distilled water @ 30 C
830.7950	Vapor Pressure	510084-04 450899-02	A	7.0×10^{-6} Pa @ 25 C

A = Acceptance; N = Not Acceptable; G = Data Gap; W = Waiver request; NA = Not applicable; II = In progress; U = Upgradeable

Pages 9-15*Manufacturing process information may be entitled to confidential treatment*

ATTACHMENT to

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DATA EVALUATION RECORD

Aceto Etoxazole Technical

STUDY TYPE: PRODUCT CHEMISTRY REVIEW

OCSPP 830.1550; 830.1600; 830.1620; 830.1670; 830.1700; 830.1750; 830.1800, 830.6302, 830.6303, 830.6304, 830.6313, 830.6314, 830.6315, 830.6316, 830.6317, 830.6319, 830.6320, 830.7000, 830.7050, 830.7100, 830.7200, 830.7220, 830.7300, 830.7370, 830.7520, 830.7550, 830.7560, 830.7570, 830.7840, 830.7950

MRIDS 51008401, 51008402, 51008403, 51008404, 45089902, 45089903

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Task Order No. Product Chem – 3-9b

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Disclaimer
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Summitec Corp. for the U.S. Environmental Protection Agency under Contract No. EP-W-16-019